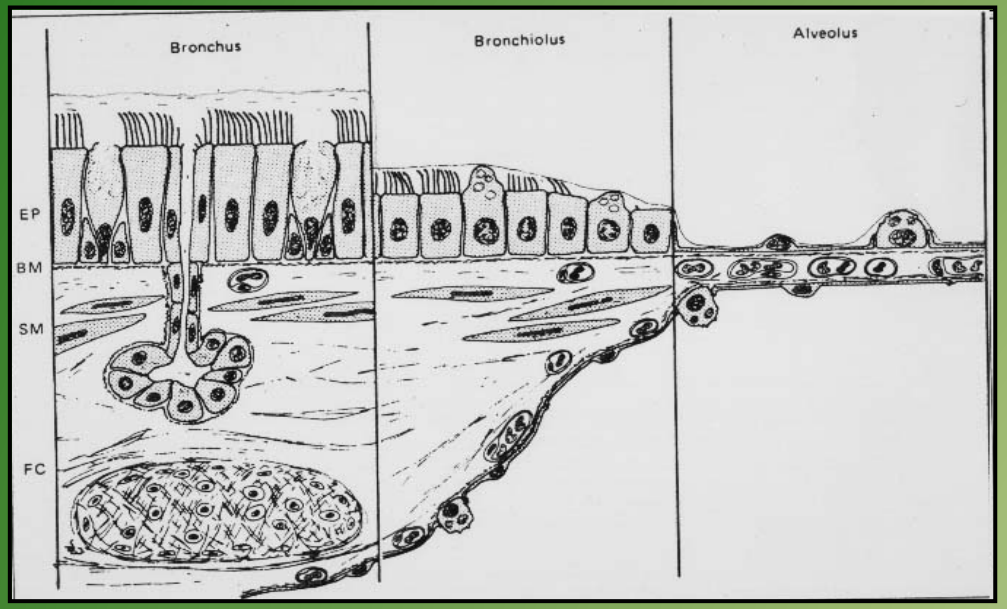
Mukomodulátor,
terapia infekcií dýchacích ciest, alebo (jednotné dýchacie cesty)

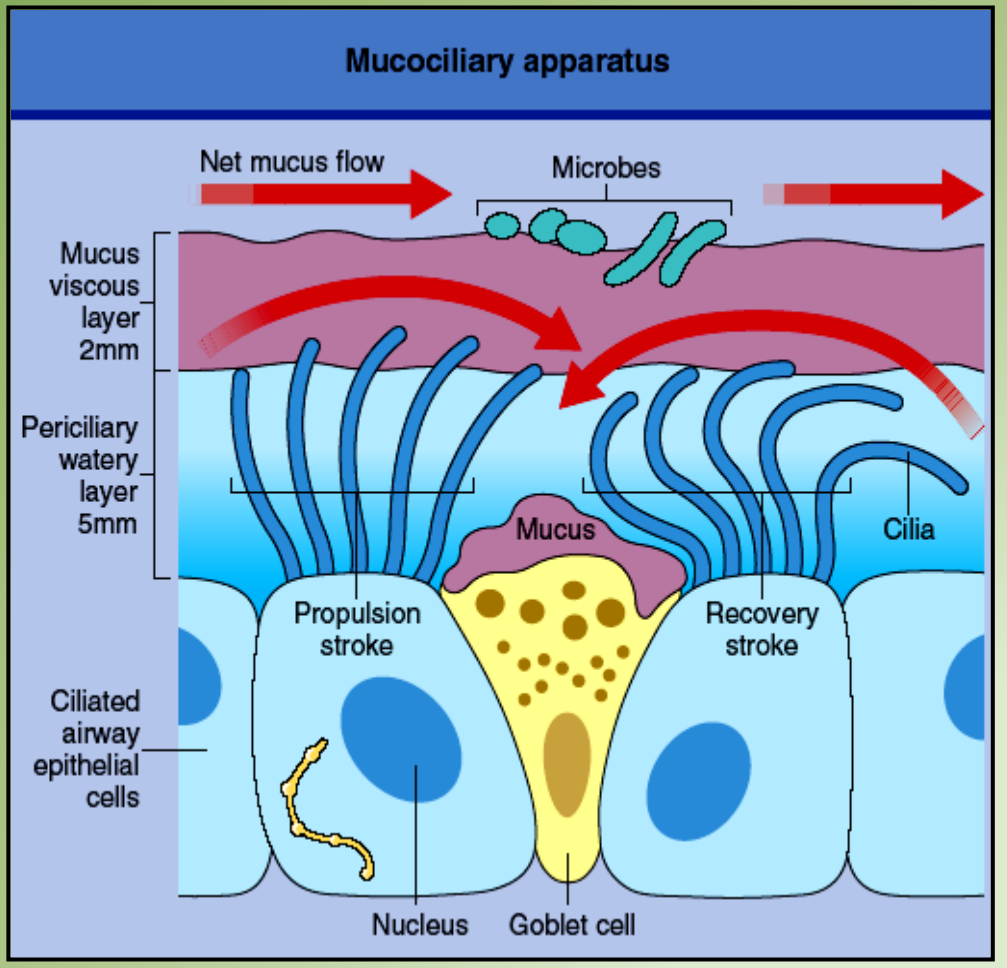
MUDr. Branko Takáč
pneumologická ambulancia
II. Detská klinika SZU B. Bystrica
btakac@dfnbb.sk

Prečo máme potrebu !

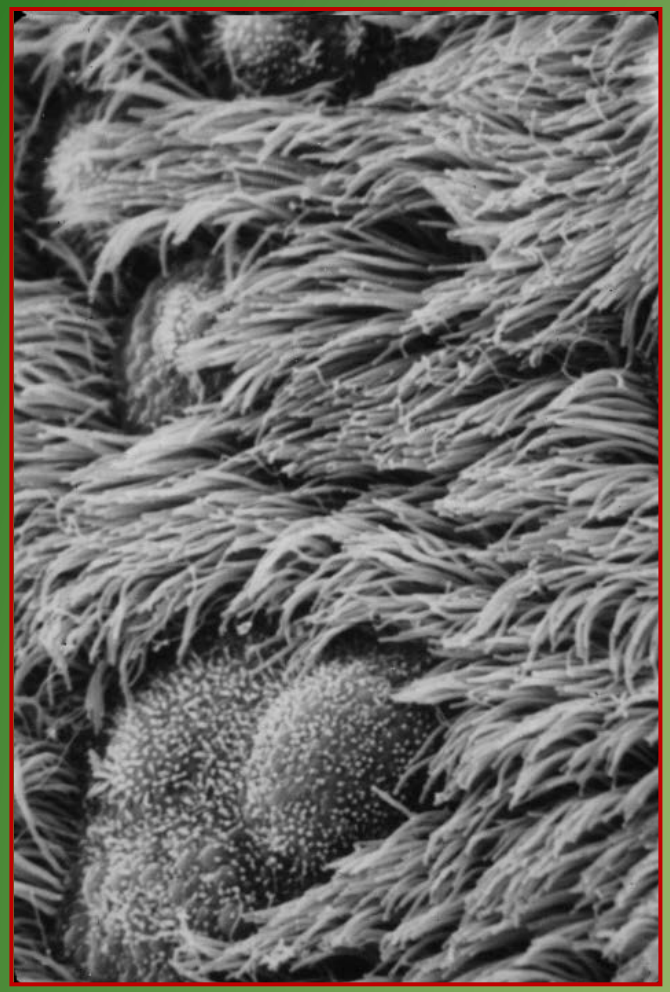
- Ide sezóna ?
- Máme nové informácie ??
- 4 je viac ako 1, 2, 3 ???

Zdravé priedušky





Choré priedušky
ČO SA TAM DEJE ?



Vírusy / baktérie / čiastočky prachu sa dostanú do DC

↓

Vznikne zápal

↓

Goblet bunky začnú produkovať viac hlienu

↓

Cílie nestačia hlien odvádzať, ich mobilita sa obmedzí

↓

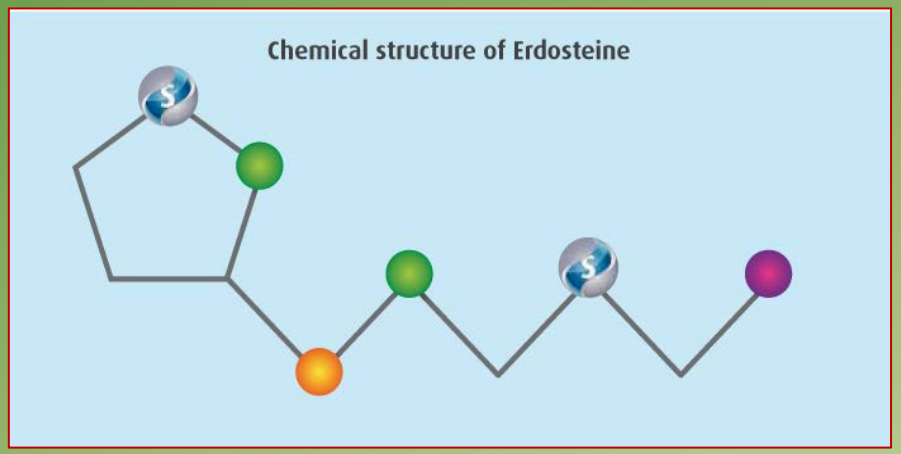
Hustý hlien = živná pôda pre ďalšie ochorenie

ERDOMED®

MUKOAKTIVÁTOR S TETRADYNAMICKÝM PÔSOBENÍM

- **MUKOMODULAČNÝM**
- **PROTIZÁPALOVÝM**
- **ANTIOXIDAČNÝM**
- **ANTIBAKTERIÁLNYM**

na liečbu akútnych a chronických ochorení dýchacích ciest u dospelých a detí so synergickým účinkom s antibiotikami [1]



Pro - aktívne liečivo stabilné pri nízkom pH, (nízka GIT toxicita)
Účinný len metabolit po first pass efekte /N-tiodiglykolyl-homocystein/
Dva tiolové mostíky štiepia disulfidové väzby glykoproteínov hlienu
Antagonizuje ROS, chráni A1-AT
Má výborný bezpečnostný profil

MUCO-MODULATORY

ANTI-OXIDANT

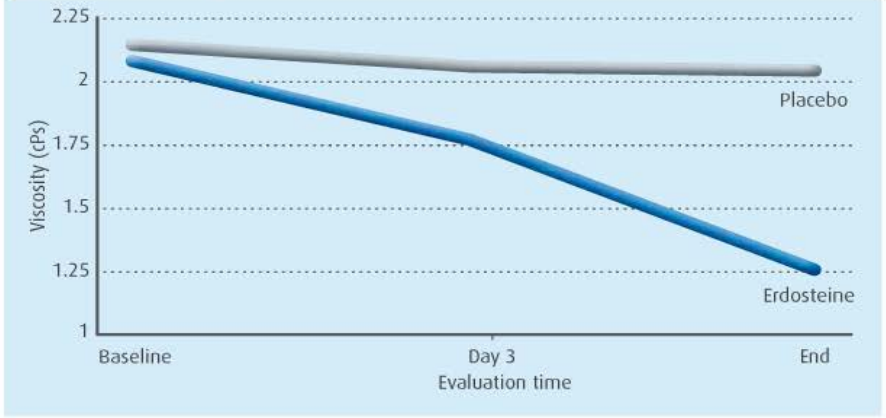
BRONCHIAL ANTI-INFLAMMATORY

BACTERIAL ANTI-ADHESION

Kontrola viskozity hlienu – zlepšenie expektorácie

Hypersecretive acute bronchitis and exacerbations of CB (chronic bronchitis) are characterized by the production of qualitatively and quantitatively altered mucus

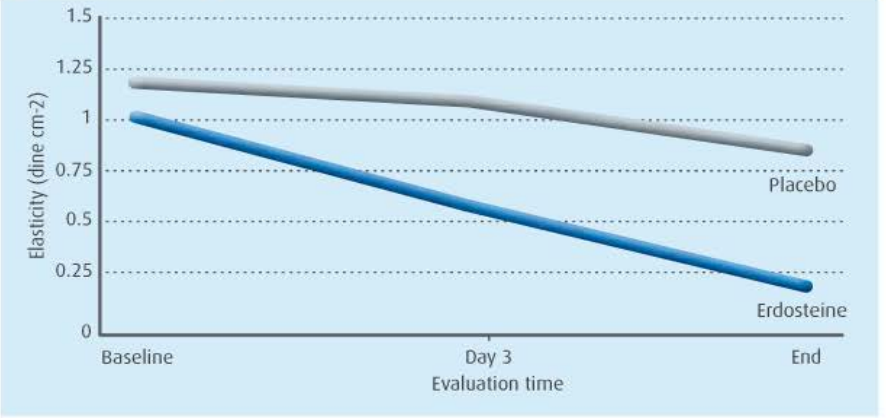
Sputum viscosity



Statistically significant **improvement of viscosity**

Mean sputum viscosity before and after treatment with Erdosteine or placebo ($p<0.001$ vs placebo)

Sputum elasticity



Statistically significant **improvement of elasticity**

Mean sputum elasticity before and after treatment with Erdosteine or placebo ($p<0.001$ vs placebo)

MUCO-MODULATORY ACTIVITY

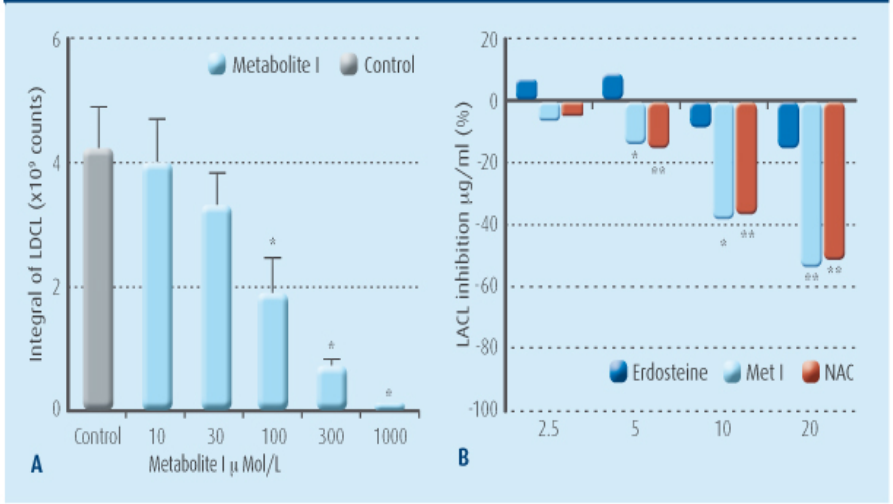
Redukcia oxidatívnych procesov- zlepšenie obranných mechanizmov

ANTI-OXIDANT ACTIVITY

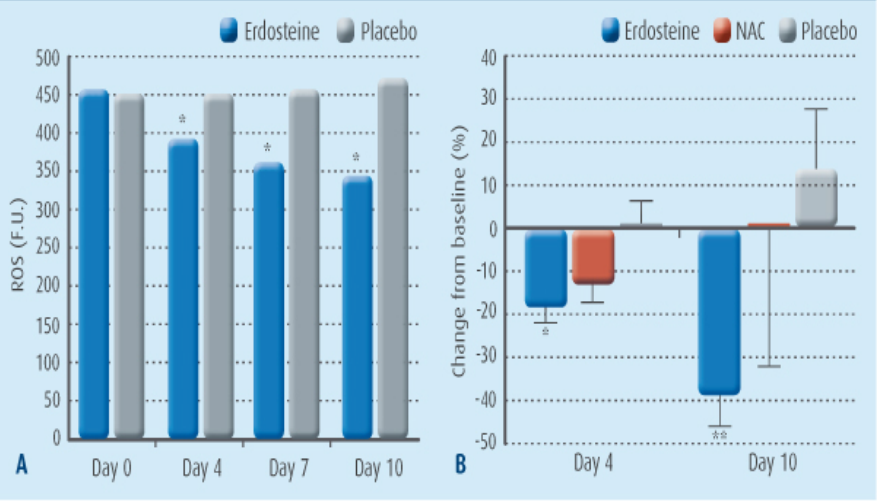
Oxidative stress is the main characteristic of CB and COPD (chronic obstructive pulmonary disease)

Erdosteine has a significant and direct activity against free radicals and lipid peroxidation

Free radical scavenging measured in vitro



Ability of Erdosteine to lower blood ROS and 8-isoprostane in COPD patients



Scavenging of reactive oxygen-derived species **(ROS)**

A. Mean integral of luminol-dependent chemiluminesce (LDCL±SD) of human neutrophils, induced by PMA, after exposure to Met I (*p<0.05 vs control)
B. Dose-dependent inhibition of human neutrophil oxidative bursts by increasing concentrations of Erdosteine, Met I and NAC (*p<0.05, **p<0.01 vs control)

Progressive reduction of biomarkers of oxidative stress and lipid peroxidation

A. ROS changes measured in subjects treated with Erdosteine and placebo for 10 days (*p<0.01 vs placebo)
B. Reduction of 8-isoprostane concentrations during a 10-day treatment with Erdosteine, NAC and placebo (*p<0.05, **p<0.001 vs placebo)

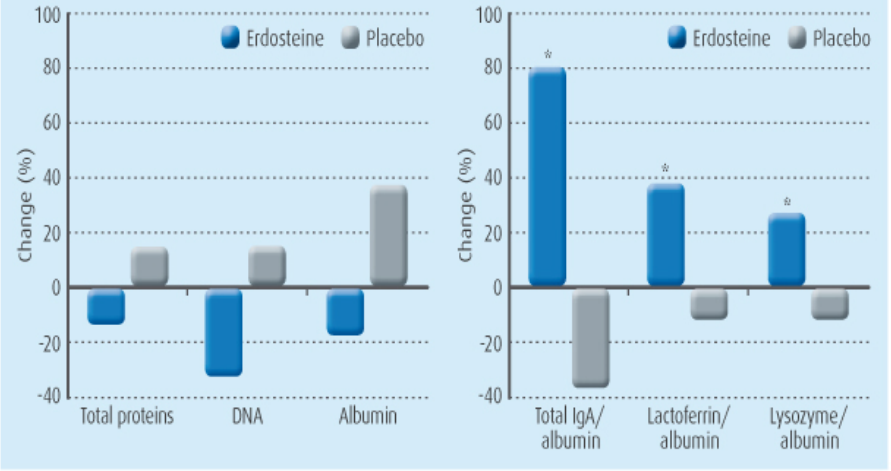
Redukcia oxidatívnych procesov - zlepšenie obranných mechanizmov

BRONCHIAL ANTI-INFLAMMATORY ACTIVITY

Chronic inflammation in CB and COPD can cause fibrosis, airway occlusion by mucus exudates, and loss of lung elasticity

Erdosteine reduces concentration of bronchial inflammatory markers and proinflammatory cytokines in sputum

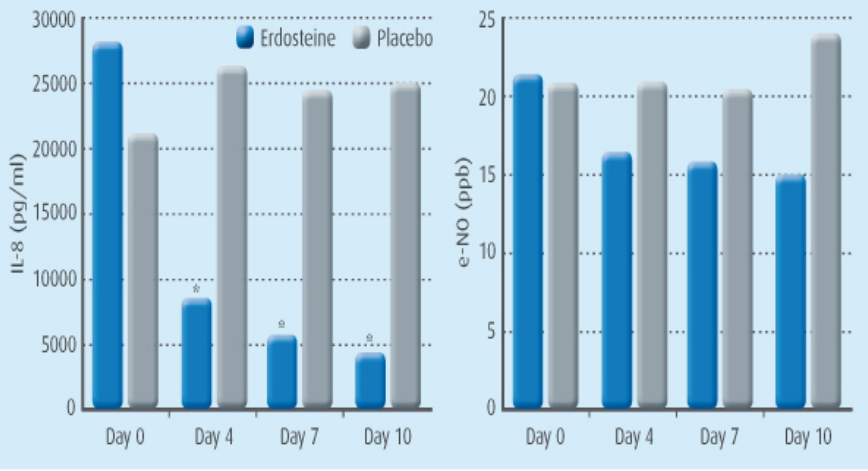
Change of some markers and relative ratio



Reduction of inflammatory markers and increase of IgA/albumin, lactoferrine/albumin, lisozime/albumin ratios in sputum

Change in various biochemical properties of sputum after treatment with Erdosteine or placebo (*p<0.05)

IL-8 and e-NO change



Reduction of pro-inflammatory cytokine IL-8 in sputum and exhaled NO (e-NO)

IL-8 and e-NO change measured in COPD patients treated with Erdosteine and placebo for 10 days (*p<0.01)

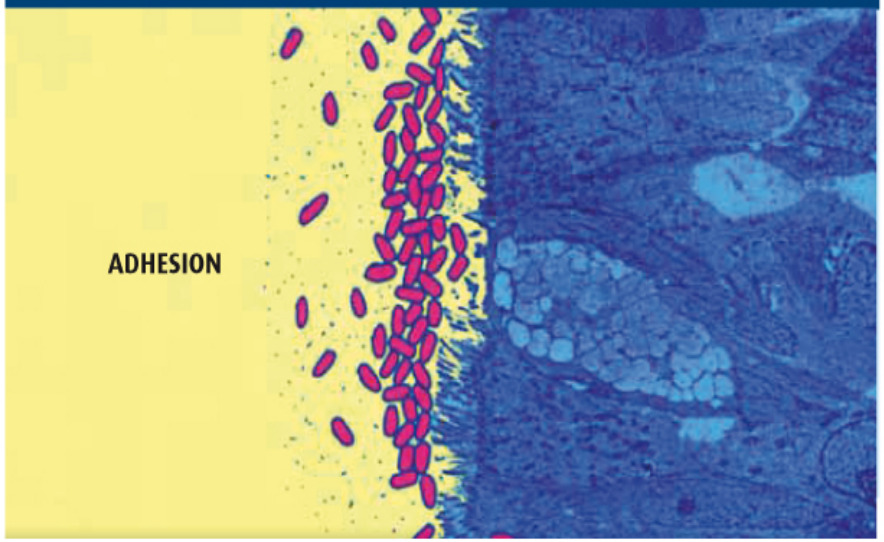
Inhibícia bakteriálnej adhézie – prevencia kolonizácie

BACTERIAL ANTI-ADHESION ACTIVITY

70% of exacerbations of CB and COPD are associated to bacterial infections

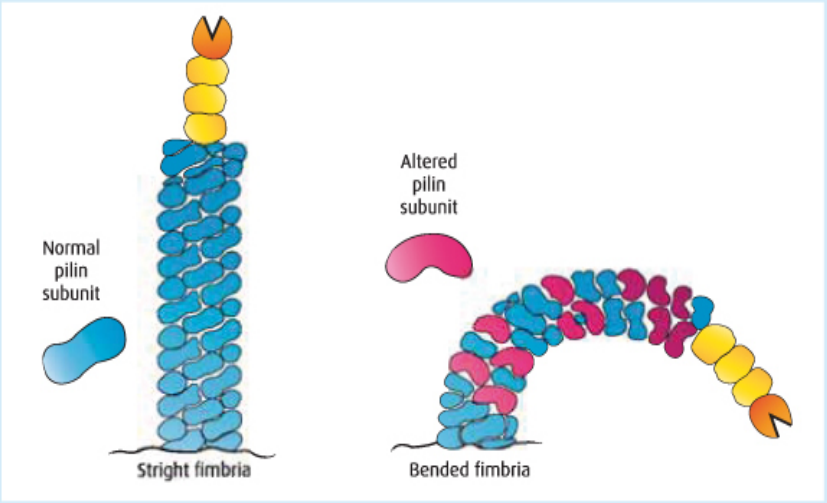
Bacterial adhesion to specific receptors located on cell surface is the initial factor which allows bacterial colonization of airways

Change of some markers and relative ratio



Specific bacterial molecules located on bacterial surface (adhesins) interact or bind with complementary epithelial cell molecules (receptors). Several filamentous appendages help bacterial adhesion to cell surface: fimbriae, pili, flagella, fibrillae

Impairment of pilin structure



Erdosteine Met I induces morphological changes of fimbriae, then interfering with binding of bacterial fi mbriae with cell receptors

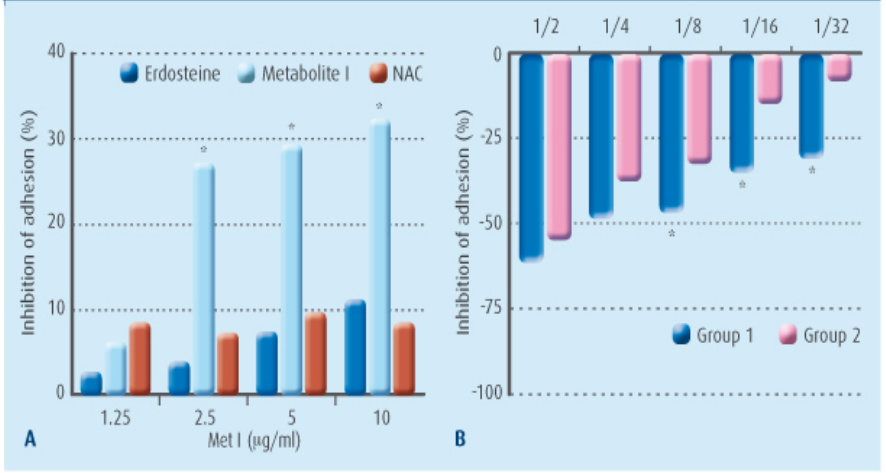
Inhibícia bakteriálnej adhézie – prevencia kolonizácie

BACTERIAL ANTI-ADHESION ACTIVITY

Improvement of anti-bacterial adhesion activity:

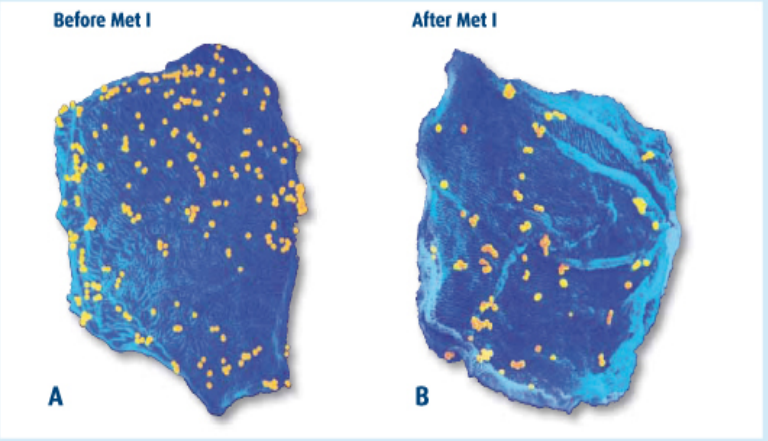
the inhibitory properties on bacterial adhesion of Clarithromycin and Ciprofloxacin are significantly increased by combination with Met I

Inhibition of Staphylococcus aureus adhesion to human mucosal cells



A. Comparative analysis of the effect of Erdosteine, Met I and NAC on S. aureus adhesion (*p<0.05)
B. Effects of sub-MICs of Clarithromycin alone (group 2) and in combination with Met I 10 µg/ml (group 1) on S. aureus adhesion (*p<0.05)

Inhibition of Staphylococcus aureus adhesion to buccal epithelial cells

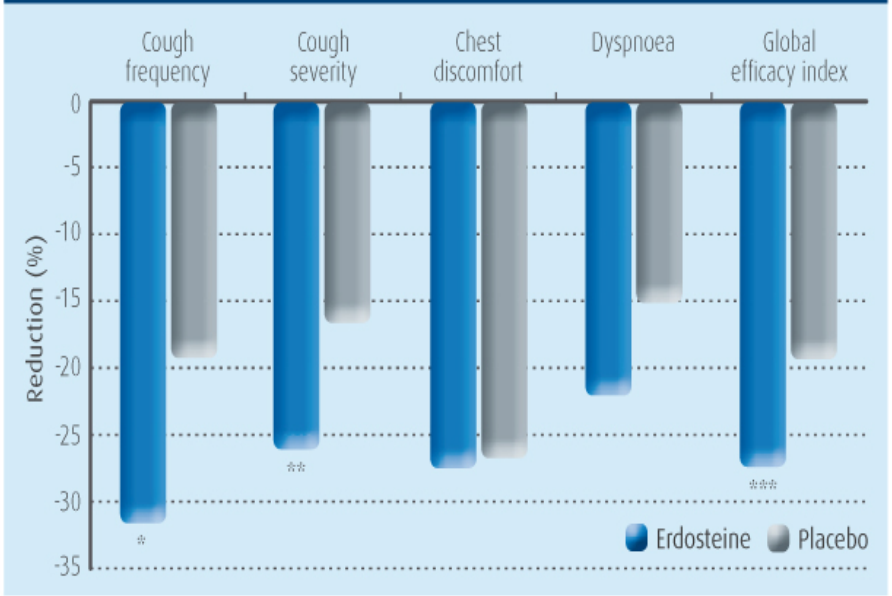


Scanning electron micrographs showing bacterial adhesion to epithelial buccal cells before (A) and after (B) the exposure of S. aureus to 2.5 µg/ml of Erdosteine Met I

Signifikantné zlepšenie respiračných symptómov

The clinical efficacy of Erdosteine has been evaluated in 50 studies involving 3540 patients with acute and chronic respiratory diseases

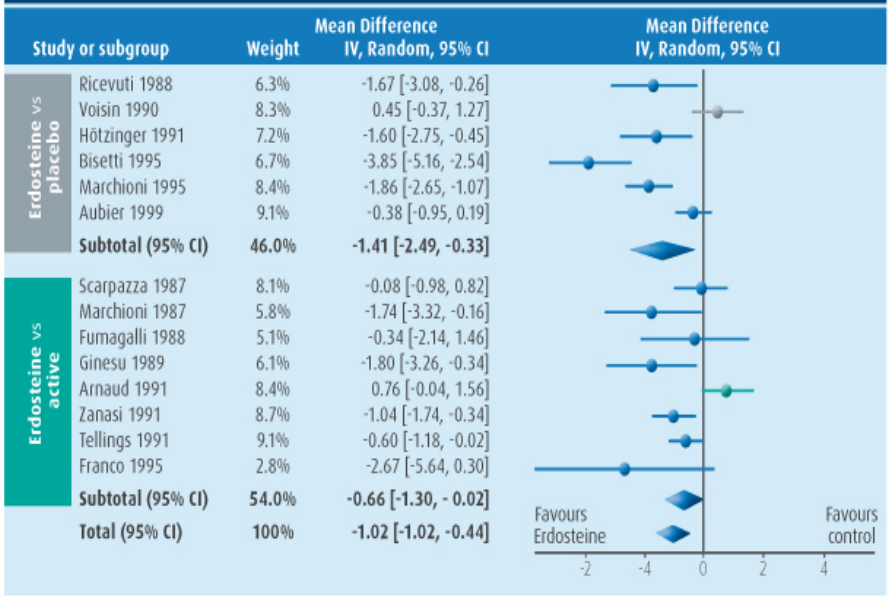
Effects of Erdosteine on clinical parameters vs placebo



Rapid and prolonged improvement of respiratory symptoms in **hypersecretive CB**

Comparison of the effects of Erdosteine and placebo on efficacy parameters in patients with stable hypersecretory chronic bronchitis (*p<0.01, **p<0.05, ***p=0.01 vs placebo)

Global Efficacy Index for respiratory symptoms



Symptoms amelioration both vs **placebo and mucolytics** in patients with CB/COPD: a meta-analysis of individual patient data **(1046)**

Meta-analysis of data from Randomized Controlled Trials comparing Erdosteine with placebo/mucolytics, given for up 10 days in association with standard therapy

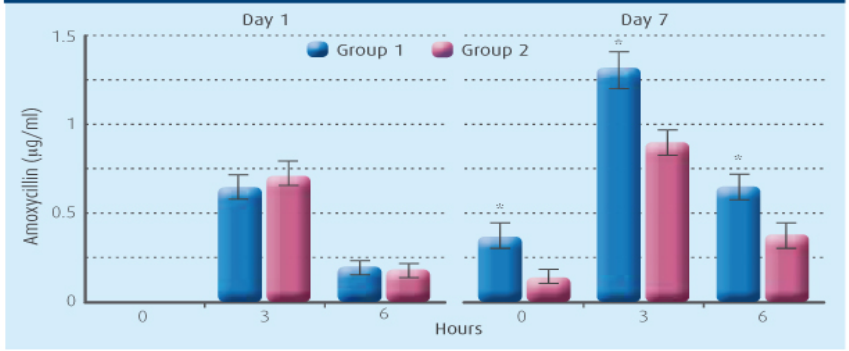
CLINICAL EFFICACY - ADULTS

Vysoký synergický efekt – redukcia exacerbácií

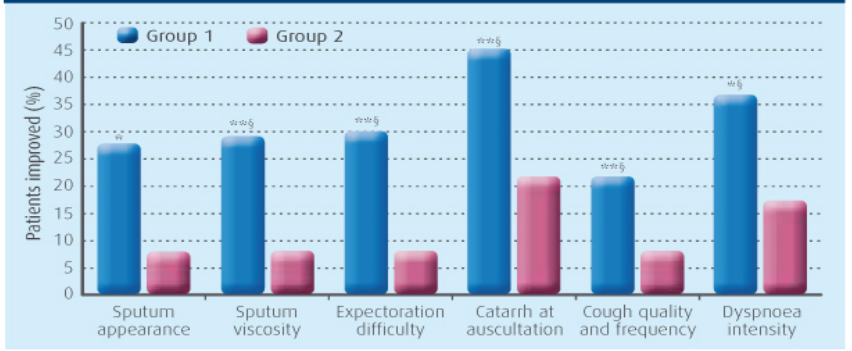
SINERGY WITH ANTIBIOTICS

Erdosteine increases sputum antibiotic concentration in patients with acute exacerbations of CB and improves the clinical situation without increasing the incidence of adverse events

Sputum Amoxycillin concentrations



Improvement of various clinical parameters in combination with Amoxycillin



Increasing of antibiotic concentrations in sputum

Sputum Amoxycillin concentrations for Amoxycillin plus Erdosteine (group 1) or Amoxycillin plus placebo (group 2) on days 1 and 7 of treatment (*p=0.05 for group 1 vs group 2)

Significant enhancing of the antibiotic activity: **faster and more favourable clinical activity** (in combination with Amoxycillin, Ampicillin and Ciprofloxacin)

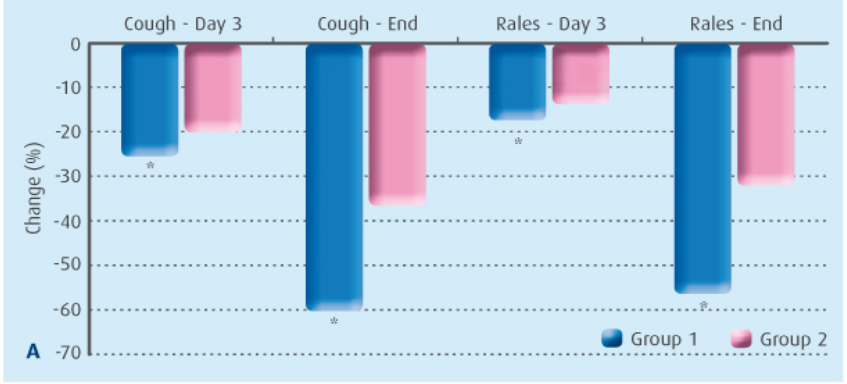
Various clinical efficacy parameters after treatment with Amoxycillin plus Erdosteine (group 1) or Amoxycillin plus placebo (group 2) (*p<0.02 at days 2-3, **p<0.01 at days 3-4, §p<0.01 at days 8-11)

Improvement of severity of symptoms in terms of mucus characteristics, cough and difficult expectoration

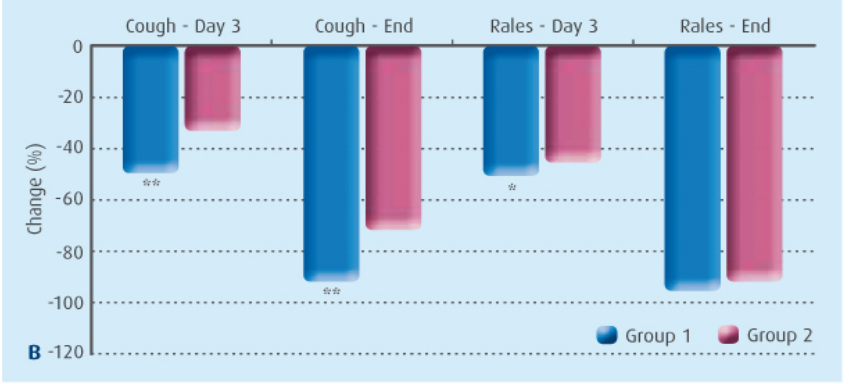
Signifikantné zlepšenie – pediatria

Efficacy of Erdosteine was evaluated in paediatric population, in different age group, with acute lower respiratory diseases

Exacerbations of CB



Statistically significant improvement of cough and rales



Reduction of the relevant symptomatology in paediatric febrile **LRTI** (lower respiratory tract infections)

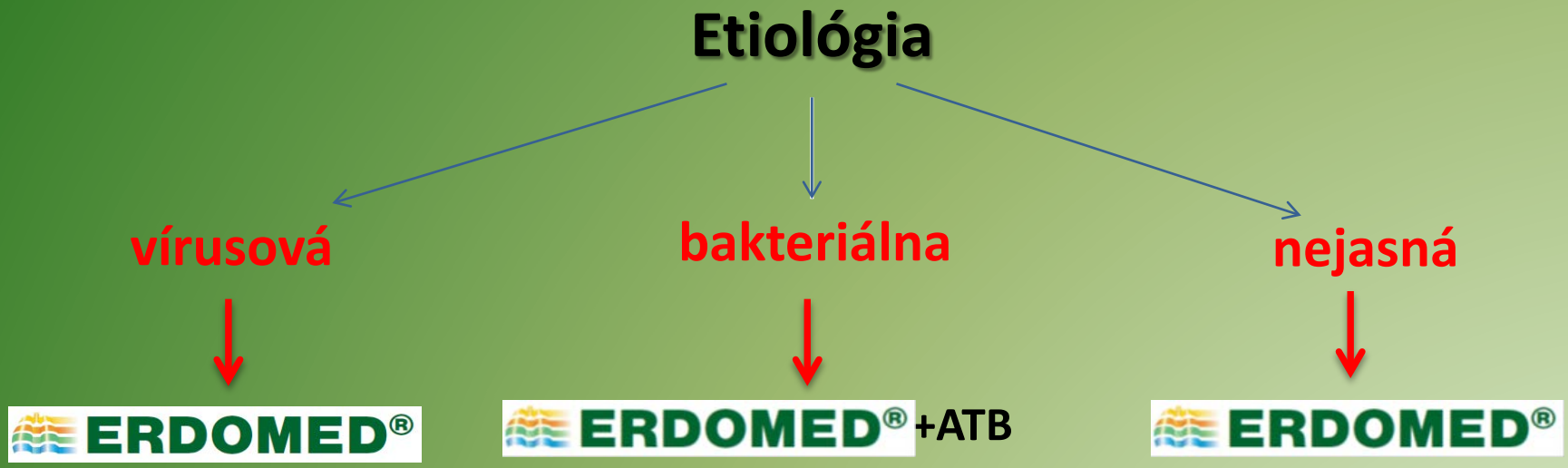
Reductions in various efficacy values/scores in paediatric patients after 3 days and at the end of treatment with:
A. Erdosteine plus Ampicillin (group 1) or placebo plus Ampicillin (group 2) *p<0.01 for both parameters between treatment
B. Erdosteine plus Amoxycillin (group 1) or placebo plus Amoxycillin (group 2) *p<0.05, **p<0.0001 vs placebo

This enhanced clinical response was achieved without compromising tolerability, since this was found to be comparable to those of the antibiotic placebo combination

CLINICAL EFFICACY - CHILDREN

- **Safety profile comparable to placebo**
- **No direct effects on gastric mucosa**
  (thiol groups blocked in acid environment)
- **No adverse events observed in children**
- **No increase of side effects in long-term treatment**
- **No interaction with other drugs**
- **No increase of side effects when combined with antibiotics**
- **Better tolerability vs NAC**
- **No increase of adverse reactions in older people and in patients with mild renal or hepatic failure**

ERDOMED - NÁVRH TERAPIE RESPIRAČNÉHO INFEKTU



Kontrola (3 - 7 dní) - pri pretrvávajúcich ťažkostiach

Erdomed je liek na lekársky predpis

"Erdosteine is the only mucolytic licensed in the UK for the symptomatic, short-term treatment of patients with acute exacerbations of chronic bronchitis "

4 je vždy viac ako 1, 2, 3 !